CLAIMS

1. A computer-implemented method for statistical analysis of QT interval as a function of changes in the RR interval before and after administration of a dose of a compound, the method comprising the steps of:

comparing a pre-dose curve of QT interval versus RR interval to a post-dose curve of QT interval versus RR interval;

determining the incidence of points of the post-dose curve that exceed an upper single-point prediction limit of the pre-dose curve to determine the degree of heterogeneity of ventricular repolarization; and

determine the magnitude that these points exceed the pre-dose QT curve and provide a quantitative assessment of treatment-induced changes in the QT-RR relationship.

2. A computer-implemented method as recited in claim 1, wherein the pre-dose curve to post-dose curve comparison step comprises the substeps of:

using an equation to fit each QT measurement to a preceding, or set of preceding, RR intervals and provide the pre-dose curve and post-dose curves; and

comparing the pre-dose and post-dose curves to determine if and at what point the post-dose curve becomes significantly higher than the pre-dose curve.

3. A computer-implemented method as recited in claim 1, wherein the compound is administered to a human.

4. A computer-implemented method as recited in claim 1, wherein the determining step comprises the substeps of:

pooling the confidence limits for the pre-dose and post-dose curves to provide an estimate of the standard error of the difference between the two curves;

using the single-point upper 95% prediction limit for the pre-dose curve to determine whether a QT point on the post-dose curve is significantly prolonged;

conducting a repeated measures test for significance to evaluate an overall effect of the treatment over all of the time periods; and

conducting individual significance tests of the proportion of prolonged outliers to determine if the treatment response is significantly higher than the pre-dose curve.

5. A computer-implemented method as recited in claim 1, wherein the step of comparing the points of the post-dose data that exceed the upper 95% single-point prediction limit to the pre-dose curve comprises the substeps of:

comparing outliers to the pre-dose curve to estimate how far above the pre-dose curve they are prolonged;

subtracting the post-dose outliers from the pre-dose curve to provide corrected ΔQT values;

comparing the corrected ΔQT values within treatment groups, post-dose to pre-dose, and across treatments;

conducting an overall test to compare the mean ΔQT of each group; and

conducting a one-sided significance test on the ΔQT values.

6. A computer readable medium that stores instructions executable by one or more processors to perform statistical analysis of QT interval as a function of changes in the RR interval before and after administration of a dose of a compound, the computer-readable medium comprising:

instructions for comparing a pre-dose curve of QT interval versus RR interval to a post-dose curve of QT interval versus RR interval;

instructions for determining the incidence of points of the post-dose curve that exceed an upper 95% single-point prediction limit to determine the degree of heterogeneity of ventricular repolarization; and

instructions for comparing the points of the post-dose data that exceed the upper 95% single-point prediction limit to the pre-dose curve to determine the magnitude of these points and provide a quantitative assessment of treatment-induced changes in the QT-RR relationship.

7. A computer readable medium as recited in claim 6, wherein the instructions for comparing the pre-dose curve to post-dose curve comprise:

instructions for using an equation to fit each QT measurement to a preceding RR interval and provide the pre-dose curve and post-dose curves; and

instructions for comparing the pre-dose and post-dose curves to determine if and at what point the post-dose curve becomes significantly higher than the pre-dose curve.

8. A computer readable medium as recited in claim 6, wherein the compound is administered to a human.

9. A computer readable medium as recited in claim 6, wherein the instructions for determining the incidence of points of the post-dose data that exceed the upper 95% single-point prediction limit comprise:

instructions for pooling the confidence limits for the pre-dose and post-dose curves to provide an estimate of the standard error of the difference between the two curves;

instructions for using the upper 95% single-point prediction limit for the pre-dose curve to determine whether a QT point on the post-dose curve is significantly prolonged;

instructions for conducting a repeated measures test for significance to evaluate an overall effect of the treatment; and

instructions for conducting individual significance tests of the proportion of prolonged outliers to determine if treatment is significantly higher than the pre-dose curve.

10. A computer readable medium as recited in claim 6, wherein the instructions for comparing the points of the post-dose data that exceed the upper 95% single-point prediction limit to the pre-dose curve comprise:

instructions for comparing outliers to the pre-dose curve to estimate how far above the pre-dose curve they are prolonged;

instructions for subtracting the data of the post-dose curve from the data of the pre-dose curve to provide corrected ΔQT values;

instructions for comparing the corrected ΔQT values between treatments; and

instructions for conducting an overall test to compare the magnitudes of each treatment ΔQT.

11. A system for statistical analysis of QT interval as a function of changes in the RR interval before and after administration of a dose of a compound, the system comprising:

a memory configured to store instructions; and

a processor configured to execute instructions for:

comparing a pre-dose curve of QT interval versus RR interval to a post-dose curve of QT interval versus RR interval,

determining the incidence of points of the post-dose data that exceed an upper 95% single-point prediction limit to determine the degree of heterogeneity of ventricular repolarization, and

comparing the points of the post-dose data that exceed the upper 95% single-point prediction limit of the pre-dose curve to determine the

magnitude of these points and provide a quantitative assessment of treatment-induced changes in the QT-RR relationship.

12. A system as recited in claim 11, wherein the instructions for comparing the pre-dose curve to post-dose curve comprise:

instructions for using an equation to fit each QT measurement data to the corresponding preceding RR interval measurement data and provide the pre-dose curve and post-dose curves; and

instructions for comparing the pre-dose and post-dose curves to determine if and at what point the post-dose curve becomes significantly higher than the pre-dose curve.

13. A system as recited in claim 11, wherein the compound is administered to a human.

14. A system as recited in claim 11, wherein the instructions for determining the incidence of points of the post-dose curve that exceed the upper 95% single-point prediction limit comprise:

instructions for pooling the confidence limits for the pre-dose and post-dose curves to provide an estimate of the standard error of the difference between the two curves;

instructions for using the upper 95% single-point prediction limit for the pre-dose curve to determine whether a QT point on the post-dose curve is significantly prolonged;

instructions for conducting a repeated measures test for significance to evaluate an overall effect of the compound over all of the time periods; and

instructions for conducting individual significance tests of the proportion of prolonged outliers to determine if any one dose of the treatment is significantly higher than the pre-dose curve.

15. A system as recited in claim 11, wherein the instructions for comparing the points of the post-dose curve that exceed the upper 95% single-point prediction limit to the pre-dose curve comprise:

instructions for comparing outliers to the pre-dose curve to estimate how far above the pre-dose curve they are prolonged;

instructions for subtracting the post-dose data from the pre-dose curve to provide corrected QT values (ΔQT);

instructions for comparing the corrected QT values within treatment groups, post-dose to pre-dose, and across treatment groups;

instructions for conducting an overall test to compare the magnitudes of each group.